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I, LISA TREVERROW, TEAM LEADER EXAMINATION SUPPORT AND SALES hereby certify that annexed is a true copy of the Provisional specification in connection with Application No. PQ 4064 for a patent by DAVID RUDOV filed on 16 November 1999.

WITNESS my hand this
Twenty-fifth day of October 2000

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ORIGINAL

PROVISIONAL SPECIFICATION

Title: SIDE EFFECTS TREATMENT

Applicant: DAVID RUDOV

The invention is described in the following statement:

SIDE EFFECTS TREATMENT

This invention relates to processes and products for the treatment of animals, including humans, to reduce side effects associated with other chemical treatment regimes.

The treatment of animals including veterinary treatment of domestic animals, sporting animals such as race horses, and livestock by use of chemical substances (including systemic and local treatments by ingestion, intravenous, and subcutaneous application as well as by external or topical application) frequently leads to undesirable side effects of the treatment regime. There is a very wide range of such side effects such as effects caused by systemic circulation of the treatment substances or caused by by-products or caused by reaction products. Such side effects include for example rashes, headaches, nausea, dizziness, vision difficulties, circulatory problems and disorders, as well as general or local sensations of pain. Other side effects include gastrointestinal problems, e.g. reflux, indigestion, gas production and eructation, constipation, diarrhoea. The side effects can be due to toxic or allergic reactions by the subject as well as being effects of the mechanisms of the substances. For example, the use of antibiotics is frequently associated with digestive problems when taken by ingestion due to the action of the antibiotics in inhibiting or killing normally present and beneficial micro-organisms in the digestive tract.

Antibiotics are frequently prescribed and used in the treatment of animals, including humans, for micro-organism infections, particularly bacterial infections and undesired side effects of the antibiotics of the general kind outlined above are observed. Such side effects frequently require separate treatment, such as treatment with antihistamines to manage mild allergic responses.

The condition known as "chronic fatigue syndrome" or "CFS" is believed to be caused or associated with bacterial infection and is therefore known to be treated with antibiotics. Undesired side effects are therefore associated with such treatment of CFS patients.

The administration of antibiotics to animals, including human patients, both before, during and after surgery or other interventions including intrusive examinations is common. Such administration of antibiotics is carried out to avoid or reduce trauma that may be commonly associated with the procedures. For example, respiratory infections, including bacterial and viral infections, are commonly encountered in post operative patients because patients are more susceptible at such times due to the immune system being compromised or more vulnerable following the traumatic procedures and due also to the condition for which the procedure has been carried out. The administration of antibiotics in such circumstances is a frequently used as a precautionary measure. The antibiotics are frequently administered intravenously together with other substances such as saline solutions, analgesics, sedatives. The administration of antibiotics or other chemical treatments as precautionary or preventative treatments before, during or after traumatic events or during immuno compromised or vulnerable conditions can be associated with the undesired side effects of the kind discussed above.

It is an object of the present invention to provide methods and products for reducing the incidence or severity of undesired side effects associated with chemical treatments of animals, including humans.

According to the present invention there is provided a method of treating an animal, including a human e.g. for a pathological or injured or abnormal condition or for precautionary or preventative treatment before during or after a traumatic event or immuno compromised or vulnerable condition of the animal, the method including a primary chemical

treatment involving the administration of a primary substance or material e.g. antibiotics or other pharmacologically effective substances for treating the animal, the administration of such substance or material being commonly or occasionally associated with undesirable side effects being experienced by the animal, the method of treating further comprising administering to the animal in conjunction with the administration of the primary treatment substance of a pharmacologically or therapeutically effective amount of a secondary substance to reduce the incidence or severity of the side effects, the secondary substance including an extract from cereal plants, the extract comprising a pharmaceutically acceptable extract derived from juice of cereal plants, preferably young plants at the unjointed stage of plant development, the extract being carried in a pharmaceutically acceptable base carrier or excipient enabling the secondary substance to be taken up by the animal being treated.

The treatment of an animal, including a human, with a primary treatment substance having undesirable side effects with the secondary substance as an adjunct to the primary treatment is based on the unexpected and surprising reduction of the incidence or severity of the side effects resulting apparently from the adjunct treatment. For example, it has been observed that in the treatment of CFS using antibiotics, the normally or occasionally expected and observed side effects of the antibiotic treatment regime were significantly reduced in subjects having the adjunct treatment with the secondary substance according to the process of the present invention.

Likewise, it has been observed that the treatment of race horses for injured or pathological conditions involving administration of chemical substances such as antibiotics, has frequently necessitated the horses being rested or "spelled" or "turned out" for several months due to side effects of the primary treatment. However the administration of a secondary substance in accordance with the present invention to the animals as an adjunct to

the primary treatment has surprisingly led to horses following thorough veterinary inspections being declared fit to be raced again after much shorter resting or spelling periods.

Broadly the secondary substance used in the present invention comprises a pharmaceutically acceptable liquid extract from a juice derived from cereal plants (which includes wild grasses) and carried in a pharmaceutically acceptable carrier or excipient for application to and take up by an animal subject. Such a substance will be referred to in this specification as "a substance of the kind described".

The references throughout this specification to a primary chemical treatment are intended to cover any treatment with a foreign substance or material, whether by external, topical, transdermal, subcutaneous, intravenous application or by ingestion, the foreign substance or material including pharmaceuticals, herbal or naturopathic substances, and organic and inorganic elements or compounds, and carriers or excipients therefor.

According to a first particular aspect of the present invention, there is provided a novel use of the substance of the kind described for the manufacture of a product for the adjunct treatment of animals including humans, to reduce the incidence or severity of side effects associated with primary chemical treatment of the animal.

According to a second particular aspect of the present invention there is provided a product for the adjunct treatment of animals, including humans, the product comprising a substance of the kind described in an effective quantity to reduce the incidence or severity of side effects associated with primary chemical treatment of the animal.

In a third particular aspect of the present invention there is provided a process for the adjunct treatment of animals including humans undergoing a primary chemical treatment, the process including the steps of administering an effective quantity of a substance of the

kind described to the animal in a manner and over a period of time to reduce the incidence or severity of side effects associated with primary chemical treatment of the animal.

In accordance with a fourth particular aspect of the present invention there is provided an adjunct secondary treatment product effective to reduce the incidence or severity of side effects associated with primary chemical treatment of the animal, the product comprising a substance of the kind described provided in a concentration and medium for administration to the animal to achieve the side effect reduction.

In a fifth particular aspect of the present invention there is provided a process for enhancing the therapeutic treatment of an animal by reducing the incidence or severity of side effects associated with primary chemical treatment of the animal, the process comprising administering to the animal a substance of the kind described in a quantity and over a period of time to be effective to achieve the side effect reduction.

Preferably in the processes of the invention the administration of the adjunct secondary treatment substance occurs simultaneously with, and may also be continued after, the primary chemical treatment period.

A substance of the kind described is already known from Australian patent specification No. AU-81985/87 (Patent No. 599725) (equivalent US Pat. No. 4,943,433) by the present applicant. In this prior patent specification, a range of possible uses of the substance are described or indicated in passing. This earlier patent specification and subsequent uses of the commercial product produced according to the prior patent specification have resulted in recognition of range of physiological indications including anti-inflammatory, immunomodulatory, and analgesic activity. However, the activity of the substance of the kind described to reduce the incidence or severity of side effects associated with primary chemical treatment of the animal is totally unexpected and surprising leading to

novel new uses of the substance hitherto unknown and with no reason to expect or suspect or seek such new uses.

Reference may be made to AU-81985/87 for further background and description of a substance of the kind described useable in the present invention in its various aspects.

References herein to "cereal plants" is to be interpreted to include wild grasses. However, a particular cereal plant found to be particularly useful as a source of the extract is *Secale Cereale* or "rye grass".

Extracts from barley and wheat are also believed to be effective. The wheat may comprise Triticum vulgare or aestivum, T. durum, T. compactum, or triticale. Corn, rice, oats, maize, sorghum and millet may also be effective.

Preferably the extract is derived from the green leafy part of the plant, or at least principally from this part of the plant although additional green parts such as stalk may be included. The leaves of the plant are preferably treated to yield the extract before the plant reaches flowering or seed production stage of development. That is, the plant is at its unjointed or immature development stage.

The extraction is preferably carried out by squeezing, crushing and/or grinding processes, not by a cutting process.

Preferably the extract from the cereal plants comprises substantially only the water soluble components of the juice.

The plant extract may be used in the concentration in which it is derived from the plants. Alternatively, if desired, the extract may be concentrated and some or substantially all the liquid content of the plant extract may be removed. For example the extracted plant matter may be dried, such as by spray drying to yield a powder for mixing with the carrier. The

spray drying is preferably carried out at a temperature of about 50°C and preferably below 60°C.

Other possible stabilisation processes for the juice include partial concentration of the derived juice to provide a concentrated liquid, freeze drying of the derived juice, and blending the derived juice with a preserving agent forming an ingredient of the carrier.

Preferably the stabilisation or mixing with the carrier or both is carried out within a short time and preferably within two hours after extraction.

In an alternative possibility the extract may be produced by firstly drying plant matter after which the dried material is comminuted to yield a powder which includes ingredients originally in the juice.

The carrier for the extract may be any suitable material such as a liquid (e.g. water or other solvent), cream, lotion, oil, gel or powder. For example the carrier may comprise a liquid in which the extract is dissolved or vanishing cream which is intended to be absorbed through the skin when applied so as to thereby carry the plant extract into sub-cutaneous tissue. A water based or aqueous carrier capable of carrying water soluble ingredients to sub-surface tissues is preferred. Benzyl alcohol is a suitable carrier component for transdermal take up of the active ingredients.

The carrier for the extract may comprise the same carrier as used for the primary chemical treatment. For example, antibiotics can be administered to an animal in a lotion or cream to be applied topically or externally. In such a case the substance of the kind described can be mixed with the primary treatment substance in the same carrier for simultaneous administration. Likewise, antibiotics or other primary treatment substances can be administered intravenously and, subject to obvious precautions concerning composition and concentrations, the substance of the kind described can be mixed with the intravenous

solution for simultaneous administration. Of course, it will be appreciated that the primary treatment substance and secondary treatment substance can be administered separately in their respective carriers, e.g. the primary substance intravenously and the secondary substance transdermally or the primary substance by ingestion and the secondary substance by sublingual administration and transdermal absorbtion through oral mucous tissues.

Preferably the carrier includes an anti-microbial agent so as to kill or at least inhibit growth, reproduction or activity of contaminating organisms that may be present in the plant extract or may be introduced during production of the substance. Preferably the anti-microbial agent is an anti-bacterial agent. In addition or alternatively the agent may have anti-fungal and anti-yeast properties. The anti-microbial agent may be added to the substance during production or may be present in the carrier if the carrier for example is a standard commercially available product. The anti-microbial agent is preferably active to inhibit any activity of organisms and thereby is operative to inhibit spoilage of the substance, e.g. spoilage of the product when being stored by the user or by a commercial outlet.

If the anti-microbial is not provided it is preferred that the extract is substantially sterile when mixed with the carrier. The plants from which the extract is derived may be grown hydroponically for example under sterile conditions to prevent the introduction of micro-organisms at that stage. The subsequent harvesting and processing may also be carried out under sterile conditions.

The ratio of the extract to the carrier may be anywhere within a large range of possible ratios. For example the ratio of base carrier to plant extract (and other additives if provided) may be anywhere between 1 to 5 and 200 to 1 (by weight). A range of 1 to 30% by weight of extract is preferred.

Preferably the substance has a generally neutral pH in the range 6.0 to 8.0. For example, the pH may be in the range 6.5 to 7.5.

Use of the substance of the kind described to reduce the incidence or severity of side effects associated with primary chemical treatment of the animal is preferably by external application so that the substance is taken up by the body by absorption through the skin or mucous tissues. A particularly preferred method of transdermal uptake is by applying the substance to the mouth for uptake through mucous tissues of the mouth. For example, the substance may be administered sublingually, e.g. in the form of drops of the substance taken orally and held in the mouth under the tongue for a short time. It is found that this method of administration is effective for uptake of the substance into the body. A suitable formulation is available commercially under the registered trade mark Oralmat, manufactured by Schumacher Pharmaceuticals Pty Ltd of Melbourne, Australia. This formulation can be taken sublingually, three drops taken three times daily, to achieve the described beneficial effects.

It may also be possible (subject to obvious safeguards concerning the composition and concentration of the substance and carrier) to administer the substance subdermally by implant or injection.

The reduction of the incidence or severity of side effects associated with primary chemical treatment of the animal was unexpected and surprising and as yet the mechanism for this activity has not been determined. Indeed no obvious possible mechanism for the observed side effect reducing activity appears from the known physiological activities of the substance according to the prior patent specification AU-81985/87 which have been seen over about the last ten years that might have suggested or predicted that activity.

The described effects of reducing incidence or severity of side effects have been observed in use of the secondary substance as a simultaneous adjunct treatment of patients being treated for chronic fatigue syndrome with a primary treatment substance in the nature of an antibiotic.

The accelerated recovery with reduced or shortened incidence or severity of side effects has been observed in race horses undergoing primary chemical treatment for injury or pathological conditions.

These observed examples of reduction of the incidence or severity of side effects in chronic fatigue syndrome patients and in race horses indicate applicability of the present invention as an adjunct treatment for an animal, including a human, being treated for a pathological or injured or abnormal condition involving administration of a primary chemical treatment, particularly antibiotics. However the observed advantageous effects in side effects reduction indicates that the present invention is also applicable as a precautionary or preventative treatment, e.g. before, during or after a traumatic event or before, during or after an observed or expected immuno compromised or vulnerable condition, e.g. pre or post operative periods. The adjunct treatment of an animal according to the present invention promises a substantial reduction or amelioration of side effects in such circumstances.

It is to be understood that various alterations, modifications and/or additions may be made to the features of the possible and preferred embodiment(s) of the invention as herein described without departing from the spirit and scope of the invention.

Dated this 15th day of November 1999

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